PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing (day/month/year)	10 JAN 2001
Applicant's or agent's file reference: 959/98	IMPORTANT NOTIFICATION

International application No.	International filing date (day/month/year)	Priority Date (day/month/year)
PCT/IL99/00440	13 AUGUST 1999	13 AUGUST 1998

Applicant
HADASIT MEDICAL RESEARCH SERVICES AND DEVELOPMENT COMPANY LTD.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	MARIANNE CRITINS
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

Form PCT/IPEA/416 (July 1992)*

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 959/38	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IL99/00440	International filing date (day/month/year) 13 AUGUST 1999	Priority date (day/month/year) 13 AUGUST 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/505 and US Cl.: 514/259		
Applicant HADASIT MEDICAL RESEARCH SERVICES AND DEVELOPMENT COMPANY LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☐ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☐ Certain observations on the international application

Date of submission of the demand 29 FEBRUARY 2000	Date of completion of this report 01 DECEMBER 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer MARIANNE CINTINS
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

Form PCT/IPEA/409 (cover sheet) (July 1998)*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/IL99/00440

I. Basis of the report

1. With regard to the elements of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-43 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of

[X] the claims:
pages 44-50 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of

[X] the drawings:
pages 1-8 , as originally filed
pages NONE , filed with the demand
pages NONE filed with the letter of

[ ] the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/fig NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/IL99/00440

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	NONE	YES
	Claims	1-14, 16-23	NO
Inventive Step (IS)	Claims	NONE	YES
	Claims	1-14, 16-23	NO
Industrial Applicability (IA)	Claims	1-14, 16-23	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-14 and 16-23 lack novelty under PCT Article 33(2) as being anticipated by Pines et al. USPN 5,449,678 A. The claims are drawn to a composition comprising an effector such as a quinazolinone derivative such as halofuginone, and a carrier, for inhibiting pathologic processes associated with tissue trauma such as cancers and fibrotic conditions by regulating the extracellular matrix economy. Pines et al. teach an antifibrotic composition with a quinazolinone -containing composition which inhibits collagen type I syntheses (see abstract). Pines et al. teach the composition useful for treating or preventing the fibrotic processes of the disorders in column 3, lines 5-41, the mechanism of action is by inhibition of collagen type I synthesis (column 3, lines 49-54).

Claims 1-14 and 16-23 lack novelty under PCT Article 33(2) as being anticipated by Nagler et al. Halofuginone - an inhibitor of collagen type I synthesis prevents postoperative formation of abdominal adhesions. Annals of Surgery. 1998. 227/4 (575-582). Nagler et al. teach halofuginone, a quinazolinone derivative and a carrier for the prevention of surgical adhesions (tissue trauma) by inhibiting collagen alpha 1 gene expression (see abstract).

Claims 1-14 and 16-23 lack an inventive step under PCT Article 33(3) as being obvious over Pines et al., USPN 5,852,024. The claims are drawn to a composition comprising an effector such as a quinazolinone derivative such as halofuginone and a carrier, for inhibiting pathologic processes associated with tissue trauma such as cancers and fibrotic conditions by regulating the extracellular matrix economy. Pines et al. teach a quinazolinone derivative such as halofuginone for inhibition or preventing both surgical and inflammatory adhesions, and in the treatment of congenital adhesions. (see abstract). The claims differ in that it does not specifically teach the composition for use in cardiac fibrosis. However, halofuginone is taught for use in inhibiting scar formation in organs such as skin, heart, lungs, liver and kidneys (column 10, lines 19-21). One of ordinary skill in the art would have known that this would work equally well for (Continued on Supplemental Sheet.)

Form PCT/IPEA/409 (Box V) (July 1998)*

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Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
cardiac fibrosis, since the composition is taught for fibrotic conditions (column 4, lines 24-27).

NEW CITATIONS

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 15

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 15 are so unclear that no meaningful opinion could be formed *(specify)*.

it is an improper multiple dependent claim under PCT Rule 6.4(a)

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.